

AMENDMENTS TO THE CLAIMS:

Claim 1 (Currently Amended): A process for the purification of olanzapine characterized in that said process comprises the following steps:

- a) mixing olanzapine with an organic acid in an organic solvent or a mixture of organic solvents to form an olanzapine acid addition salt,
- b) precipitating and isolating the olanzapine acid addition salt and,
- c) ~~transformation~~ transforming of the olanzapine acid addition salt to olanzapine, wherein the transformation step comprises the following substeps:
 - i) dissolving ~~an~~ the acid addition salt of olanzapine in water to make a solution thereof ~~to form an aqueous solution thereof~~,
 - ii) adjusting the pH of the obtained ~~aqueous~~ solution to about 8-10,
 - iii) contacting the adjusted pH aqueous solution with an organic solvent to form a separate water phase and organic solvent phase;
 - ~~iiiiv)~~ extracting olanzapine from the aqueous water phase to an the organic solvent phase;
- and
- ivv) ~~isolating the acid addition salt of olanzapine from the organic solvent phase by concentrating the solution to form olanzapine salt crystals therein~~ organic solvent phase to cause olanzapine crystals to form therein and separating and separation of the crystals of the aforementioned salt of olanzapine therefrom from the organic solvent phase;
wherein the olanzapine crystals include less than 0.05 % of piperazine 1,4-bis-4-yl-(2-methyl)-10H-thieno-[2,3-b][1,5]benzodiazepine.

Claim 2 (Currently Amended): The process according to claim 1 wherein the organic acid in step (a) is selected from the group consisting of ~~one or more~~ sulfonic acids ~~or one or more~~ and carboxylic acids.

Claim 3 (Currently Amended): The process according to claim 2 wherein the ~~one or more~~ carboxylic acid[[s]] are ~~is~~ selected from the group consisting of ~~one or more of~~ fumaric acid and benzoic acid.

Claim 4 (Currently Amended): The process according to claim 1 wherein the organic solvent in step (a) is selected from the group consisting of ~~one or more of~~ tetrahydrofuran, acetone, dimethylformamide and acetonitrile.

Claim 5 (Previously Presented): The process according to claim 1 wherein the mixture of organic solvents in step (a) is a mixture of tetrahydrofuran with at least one polar solvent.

Claim 6 (Currently Amended): The process according to claim 5 wherein said polar solvent is selected from the group consisting of ~~one or more of~~ dimethylformamide, dimethylacetamide, N-methylpyrrolidone, 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone, 1,3-dimethyl-2-imidazolidinone, tetramethylurea, dimethyl sulfoxide, sulfolane, acetone and acetonitrile.

Claims 7-21 (Cancelled)

Claim 22 (Currently Amended): A process for the preparation of olanzapine ~~in the form of an acid addition salt~~ characterized in that said process comprises the following steps:

a) reacting 4-amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride with N-methylpiperazine to yield olanzapine and

b) ~~transforming~~ converting the obtained olanzapine to an acid addition salt thereof, ~~wherein the transformation step comprises the following substeps:~~

~~i) diluting the obtained reaction mixture with water;~~

~~ii) extracting the diluted reaction mixture with an organic solvent, wherein the organic solvent is selected from the group consisting of ketones, chlorinated hydrocarbons, and mixtures thereof;~~

~~iii) evaporating the organic phase and diluting the residue with a second solvent to obtain a solution containing the residue,~~

~~iv) adding an organic acid to the solution containing the residue to precipitate olanzapine acid addition salt therefrom and~~

~~v) isolating precipitated olanzapine acid addition salt by formation and separation of crystals from the solution; and~~

c) transforming the olanzapine acid addition salt to olanzapine, wherein the transformation comprises the following substeps:

i) dissolving the acid addition salt of olanzapine in water to form an aqueous solution thereof;

ii) adjusting the pH of the aqueous solution to about 8-10,

iii) contacting the adjusted pH aqueous solution with an organic solvent to form a water phase and an organic phase;

iv) extracting olanzapine from the water phase to the organic solvent phase;

v) isolating olanzapine from the organic solvent phase by concentrating the solution to cause formation of crystals of olanzapine therein followed by separation of the crystals therefrom; and

wherein the olanzapine crystals include less than 0.05 % of piperazine 1,4-bis-4-yl-(2-methyl)-10H-thieno-[2,3-b][1,5]benzodiazepine.

Claim 23 (Cancelled).

Claim 24 (Currently Amended): A process for the preparation of olanzapine ~~in the form of an acid addition salt~~ characterized in that said process comprises the following steps:

a) reacting N-desmethyloanzapine ~~is reacted~~ with a methylating agent to yield a reaction mixture containing olanzapine,

b) diluting the obtained reaction mixture ~~is diluted~~ with water and acidified ~~acidifying the mixture, as necessary,~~ with an acid,

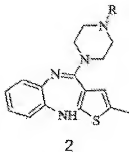
c) ~~adding to the reaction mixture,~~ a chlorinated organic solvent ~~is added to provide separable aqueous to the diluted reaction mixture to induce formation of separate acidic water and organic solvent phases which wherein olanzapine is contained in the water phase are then separated,~~

d) separating the water and organic solvent phases;

e) neutralizing the obtained aqueous water phase is neutralized and extracting olanzapine ~~is extracted therefrom~~ with a chlorinated organic solvent to obtain the organic solvent phase containing olanzapine and

f) adding an organic acid or substituted organic acid or an organic acid derivative of formula RX; wherein R represents an organic radical and X is selected from a group of Cl, Br or

I; or an organic acid anhydride; is added to the organic phase to form a N substituted N-desmethylolanzapine derivative of formula 2



~~fg) optionally evaporating the obtained organic solvent phase is optionally evaporated and diluting the residuc~~ is diluted with a second organic solvent,

~~gh) adding an organic acid is added either to the obtained-diluted residuc~~ solution containing the second organic solvent ~~and residuc therein~~ or directly to the olanzapine extract from ~~the said extraction in step (d), and~~

~~hi) precipitated-precipitating an olanzapine acid addition salt is isolated by separation of the in the form of crystals from the material to which an organic acid was added in step h; and~~

~~ij) transformation-of-transforming the olanzapine acid addition salt to olanzapine, wherein the transformation step comprises the following substeps:~~

- ~~1) dissolving an acid addition salt of olanzapine in water,~~
- ~~2) adjusting pH of the obtained solution to about 8-10,~~
- ~~3) extracting olanzapine from the water phase to the organic solvent phase and~~
- ~~4) isolating the acid addition salt of olanzapine from the organic solvent phase by concentrating the solution and separation of the crystals~~

~~wherein the obtained olanzapine includes less than 0.05 % of piperazine 1,4-bis-4-yl-(2-methyl)-10H-thieno-[2,3-b][1,5]benzodiazepine.~~

Claim 25 (Cancelled)

Claim 26 (Previously Presented): The process according to claim 24 wherein said chlorinated organic solvent is methylene chloride.

Claim 27 (Original): The process according to claim 24 wherein the organic solvent in steps (c) and (d) is methylene chloride and said second solvent in step (f) is methanol.

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Claims 28-34 (Cancelled)

Claim 35 (Currently Amended): Olanzapine prepared according to the processes disclosed in claim 1 characterized in that the ~~detectible~~ N-desmethylolanzapine content, if any, in the final product of olanzapine is less than 0.1 %.

Claim 36 (Currently Amended): Olanzapine prepared according to the processes disclosed in claim 1 that contains ~~a detectable amount, if any, of~~ less than 0.05 % of piperazine 1,4-bis-4-yl-(2-methyl)-10H-thieno-[2,3-b][1,5]benzodiazepine.

Claims 37-43 (Cancelled)